Targeted Research Area: Asthma and Respiratory Illnesses

General Information on Asthma and Respiratory Illnesses

- **Prevalence and incidence of asthma:**
  - The reported prevalence of asthma has increased dramatically in children and adults over the past decade. An estimated 4.8 million children in the United States (1 in 15) under the age of 18 have asthma.[1]
  - The epidemic of asthma and allergic disorders is occurring in western societies / First World countries. [2]
  - Asthma rates have increased by 160% in the past 15 years in children under the age of 5.[3]

- **Mortality from asthma:**
  - The death rate from asthma for children ages 19 and younger increased by 78% between the years 1980 and 1993.[4]
  - Nearly 300 children die each year from asthma.[5]

- **Disease severity/disease burden:**
  - Each year 150,000 children are hospitalized for asthma.[6]
  - Asthma is a leading cause of school absenteeism, resulting in 10 million missed school days per year. It often causes interrupted sleep, limited activity, and disruptions of family and caregiver routines.[7]
  - Severity of the disease has increased as seen in increased hospitalization rates. One study found that the odds of an adverse outcome (i.e., intubation, cardiopulmonary arrest, or death) among children hospitalized for asthma in California doubled between 1986 and 1993. [8]
  - Two surveys found that many inner city children took no medication for their asthma, despite frequent symptoms, ER visits, and absences from school. Inner city children who are on medications for asthma rely heavily on beta adrenergic agonists alone, which could lead to more unstable asthma. In one study of inner city children with asthma, 18% of the children were reported to have low birth

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1 Environmental Protection Agency. *Asthma and Upper Respiratory Illnesses*. Available at http://www.epa.gov/children/asthma.htm

2 Abramson MJ, Walters EH. The epidemic of asthma: too much allergen or not enough infection? Medical Journal of Australia 2000;172(3):119-21.

3 Environmental Protection Agency. *Asthma and Upper Respiratory Illnesses*. Available at http://www.epa.gov/children/asthma.htm

4 Centers for Disease Control and Prevention, National Center for Environmental Health. *Asthma's Impact on Children And Adolescents*. Available at http://www.cdc.gov/nceh/airpollution/asthma/children.htm

5 Environmental Protection Agency. *Asthma and Upper Respiratory Illnesses*. Available at http://www.epa.gov/children/asthma.htm

6 Ibid.

7 President's Task Force on Environmental Health Risks and Safety Risks to Children. *Asthma and the Environment: A Strategy to Protect Children*. Available at http://epa.gov/children/whatwe/fin.pdf

8 Pandya R, Solomon G, Kinner A, Balmes JR. Diesel exhaust and asthma: hypotheses and molecular mechanisms of action. Environmental Health Perspectives 2002;110 (Suppl 1):103-12.

weight, 25% were in an intensive care unit at birth, and 10% were on a respirator.[9]

- **Cost to individual/family/society/healthcare system:**
  - In the U.S., the estimated annual cost of treating asthma in children under the age of 18 is $3.2 billion.[10]

- **Special populations**
  - Asthma-related hospitalizations for inner-city and minority children have risen disproportionately.[11]
  - Minority populations also suffer a disproportionately higher rate of death from asthma. In 1995, the death rate for asthma in African-American children was four times the death rate in Caucasian children.[12]
  - There are racial differences in prevalence even when adjusting for socioeconomic factors. According to NHANES II data, the rate of asthma in children 6 months to 11 years of age was 3% in Caucasians and 7.2% in African-Americans. The greatest increase in prevalence has been reported among inner-city children and young adults living in the U.S. African-American children have higher prevalence, even when adjusting for socioeconomic factors. [13]

Hypotheses 1 – 5, described on the following pages, are associated with the Asthma and Respiratory Illnesses targeted research area.

[9] Eggleston PA, Buckley TJ, Breysse PN, Wills-Karp M, Kleeberger SR, Jaakkola JJ. The environment and asthma in U.S. inner cities. Environmental Health Perspectives 1999;107(Suppl 3):439-50.

[10] American Lung Association. *Asthma in Children Fact Sheet (March 2002).* Available at: http://www.lungusa.org/asthma/ascpedfac99.html

[11] Environmental Protection Agency. *Asthma and Upper Respiratory Illnesses.* Available at http://www.epa.gov/children/asthma.htm

[12] President's Task Force on Environmental Health Risks and Safety Risks to Children. *Asthma and the Environment: A Strategy to Protect Children*. Available at http://epa.gov/children/whatwe/fin.pdf

[13] Eggleston PA, Buckley TJ, Breysse PN, Wills-Karp M, Kleeberger SR, Jaakkola JJ. The environment and asthma in U.S. inner cities. Environmental Health Perspectives 1999;107(Suppl 3):439-50.

Hypothesis #1: Infections in early childhood have a protective effect against asthma.

General Information Related to Hypothesis #1

- **Frequency/load of exposure to daycare-related infections**: In 1995, approximately 60% of children in the U.S. were attending day care. Day care attendance is associated with an increased risk of infections.[14]
- **Frequency/Load of exposure to infections:** Children in First World countries now suffer fewer infections as a result of improved hygiene, smaller families, and effective early-childhood vaccination programs. Another factor that has led to reduced exposure to infections has been the use of antibiotics in early childhood.[15]
- **Findings from recent research (targeted search):** Information reported in the following four studies contributed to the above-mentioned hypothesis.

Study #1: Celedon JC, Litonjua AA, Ryan L, Weiss S, Gold DR. Day care attendance, respiratory tract illnesses, wheezing, asthma, and total serum IgE level in early childhood. Archives of Pediatrics & Adolescent Medicine 2002;156(3):241-5.

Study #1 hypothesis being tested: Day care-related infections in the first year of life are protective against wheezing and asthma in the first four years of life among children with a parental history of atopy.

Study #1 findings: The study found that day care attendance in early life was protective against the development of atopy by 2 years of age. However, there was no significant association between day care attendance in the first year of life and recurrent wheezing or asthma at 4 years of age. A protective effect of day care attendance in early life against wheezing may not be observed until after 4 years of age. The authors state that the lack of an inverse association between day care attendance and asthma or wheezing in early childhood is likely because wheezing in early childhood may be related to infections in children with small airways or to allergic inflammation of the airways. Because of the increased risk of respiratory infections associated with day care attendance in the first year of life (but inverse association with atopy), it may be impossible to observe a protective effect of day care attendance on wheezing until the children are older. The authors call for further follow-up study on their cohort to help clarify the relation between day care attendance and or respiratory tract illnesses in early life and childhood asthma and atopy.

[14] Celedon JC, Litonjua AA, Ryan L, Weiss S, Gold DR. Day care attendance, respiratory tract illnesses, wheezing, asthma, and total serum IgE level in early childhood. Archives of Pediatrics & Adolescent Medicine 2002;156 (3):241-5.

[15] Droste JH, Wieringa MH, Weyler JJ, Nelen VJ, Vermeire PA, Van Bevers HP. Does the use of antibiotics in early childhood increase the risk of asthma and allergic disease? Clinical and Experimental Allergy 2000;30:1547-53.

Study #2: Illi S, vonMutius E, Lau S, Bergmann R, Niggemann B, Sommerfeld C, Wahn U. Early childhood infectious diseases and the development of asthma up to school age: a birth cohort study. BMJ 2001;322:390-5.

Study #2 hypothesis being tested: Infections in early childhood have a protective affect against asthma.

Study #2 findings: The study found that the total burden of infection as well as certain viral infections, namely repeated episodes of runny nose and viral infections of the herpes type, before age 3 were shown to have an inverse relation with the development of asthma by age 7. However, the study also found that repeated lower respiratory tract infections early in life were positively associated with the subsequent development of asthma. The authors suggest that viral infections other than lower respiratory tract infections early in life may stimulate the immature immune system towards the Th1 phenotype, reducing the risk for developing asthma up to school age. The authors further suggest there is a window of vulnerability, with the immature immune system being most susceptible to the influence of infections with the first year of life.

Study #3: Abramson MJ, Walters EH. The epidemic of asthma: too much allergen or not enough infection? Medical Journal of Australia 2000;172(3):119-21.

Study #3 hypothesis being tested: The absence of infection in childhood might increase the risk of atopy. Childhood infections seem to be important in normal maturation of the immune system (Th1 immunity), with asthma as a manifestation of a persistent "immature" immune system.

Study #3 findings: Studies of cohorts that have survived infections such as measles and tuberculosis, have shown a reduced risk of atopy and asthma. However, the role of vaccinations in relation to infections is still not clear. The authors suggest that the relative absence of immunologically modifying childhood infections or environmental adjuvants is likely to be a factor in the epidemic of asthma and allergic disorders in Western societies. Further, the authors identify a need for research on the role of vaccinations, and research to confirm effects of antibiotic use and determine associated immunological mechanisms responsible.

Study #4: Droste JH, Wieringa MH, Weyler JJ, Nelen VJ, Vermeire PA, Van Bevers HP. Does the use of antibiotics in early childhood increase the risk of asthma and allergic disease? Clinical and Experimental Allergy 2000;30:1547-53.

Study #4 hypothesis being tested: The use of antibiotics in the first year of life may lead to subsequent development of asthma and allergic disorders.

Study #4 findings: The prevalence of asthma, hay fever, and eczema were significantly higher in children who used antibiotics in the first year of life and who had a parent with hay fever. For children without parental hay fever, there were no significant associations between antibiotic use and asthma or allergy. The study supported the hypothesis that the use of antibiotics in the first year of life was shown to be significantly

associated with the development of asthma only in children who are predisposed to atopic immune responses. The authors suggest that prospective studies should be conducted in populations with different "risk levels" of asthma and allergic disorders to better understand the association between early childhood infections and development of asthma and the role of genetic factors in this process.

Hypothesis #2: Endotoxin exposure in childhood may have a protective effect against the development of asthma.

General Information Related to Hypothesis #2

- **Findings from recent research (targeted search):** Information reported in the following three studies contributed to the above-mentioned hypothesis.

Study #1: Liu AH. Endotoxin exposure in allergy and asthma: Reconciling a paradox. Journal of Clinical Immunology 2002;109(3):379-92.

Study #1 hypothesis being tested: Endotoxins may have a positive as well as a negative effect on development of asthma.

Study #1 findings: Some studies indicate that endotoxins have a protective effect against the development of asthma, supporting the hypothesis that microbial exposures promote the Th1-type immune development. Endotoxin exposure in farming communities, for example, has been associated with a reduced risk of asthma. However, there are also studies pointing to the negative influence of endotoxin exposure. Some studies have shown that endotoxins can induce varying degrees of airflow obstruction and neutrophil inflammation in non-asthmatic subjects. The author suggests that studies of endotoxin exposure and asthma hint that the benefits of exposure depend on the importance of timing, dosage, environmental cofactors, and genetics. The author calls for more research, particularly for prospective studies in different locales, to better determine the role of endotoxin exposure.

Study #2: Douwes J, Pearce N, Heederik D. Does environmental endotoxin exposure prevent asthma? Thorax 2002;57(1):86-90.

Study #2 hypothesis being tested: Respiratory exposure to endotoxins may confer a protective effect against development of atopy and asthma.

Study #2 findings: A few studies have demonstrated a protective effect of endotoxins against atopy through promotion of the Th1 pathway of the immune system during fetal and perinatal development. However, other studies show that endotoxin exposure can exacerbate pre-existing asthma and may be a causal factor in development of non-allergic asthma. The authors suggest that caution should be taken regarding the hypothesis. A protective effect has only been established for atopy. Exposure to endotoxins may prevent primary causation of allergic asthma, but it may be both a primary and secondary cause of non-allergic asthma. The study's findings suggest that the discrepancy in the role of endotoxins may be related to the timing (prenatal and neonatal vs. child and adult life) and dose of exposure. The authors call for further research on these aspects of endotoxin exposure.

Study #3: Kilpelainen M, Terho EO, Helenius H, Koskenvuo M. Farm environment in childhood prevents the development of allergies. Clinical and Experimental Allergy 2000 Feb;30(2):201-8.

Study #3 hypothesis being tested: A farm environment has a protective effect on asthma, wheezing, and atopic disorders.

Study #3 findings: The study found that childhood farm environments reduced the risk for physician-diagnosed asthma and episodic wheezing analyzed together. The study suggests that childhood farm environments have a protective effect against allergic rhinitis and/or conjunctivitis, and more weakly against asthma and wheezing, irrespective of family size. Environmental exposure to immune modulating agents, such as environmental mycobacteria and actinomycetes, favoring manifestation of a non-atopic phenotype (Th1) could explain this finding. The authors suggest that more research is needed to study interactions between exposure to microbes and asthma.

Hypothesis #3: Maternal exposures to environmental agents (e.g., indoor allergens or environmental tobacco smoke), behaviors (e.g., diet, history of asthma) or complications (e.g., early labor, maternal health complications) during pregnancy may contribute to the development of asthma and other respiratory illnesses in offspring.

General Information Related to Hypothesis #3

- **Frequency/load of exposure to environmental tobacco smoke (ETS) and the effect of maternal diet:** ETS exposure has decreased significantly in the past two decades, even amongst smoking parents. Asthma development may be the result of an increasing decline in host resistance due to reduced consumption of fruit and vegetables and resulting vitamin deficiencies.
- **Findings from recent research (targeted search):** Information reported in the following six studies contributed to the above-mentioned hypothesis.

Study #1: Annesi-Maesano I, Moreau D, Strachan D. In utero perinatal complications preceding asthma. Allergy 2001;56:491-97.

Study #1 hypothesis being tested: Various in utero and perinatal influences contribute to the development and severity of asthma in childhood.

Study #1 findings: Controlling for confounders that predispose one to health complications in pregnancy or child asthma (including premature birth and its associated complications), the study found that maternal health complications during pregnancy, labor, or delivery, as well as neonatal illness in the first week of life were associated with a risk of a child developing asthma. In particular, the risk increased with early and threatened labor and malpresentation and malposition of the fetus. The results provide further evidence that in utero and perinatal complications may increase the risk of developing asthma. Unidentified processes that lead to some of these complications may be associated with fetal "programming," whereby a stimulus or insult at a critical period of development leads to permanent effects on the body's structure, physiology, and metabolism. The authors suggest that more detailed studies of specific perinatal complications are needed, as well as studies of how genetic and early life factors interact with the developing lung and lead to the onset of asthma.

Study #2: Nafstad P, Magnus P, Jaakkola JJK. Risk of childhood asthma and allergic rhinitis in relation to pregnancy complications. Journal of Allergy and Clinical Immunology 2000;106(5):867-73.

Study #2 hypothesis being tested: Events occurring during fetal life may affect the development of the immune and respiratory systems and increase the risk of asthma and allergic diseases. The study further hypothesized that complications related to the pathophysiology of the uterus (e.g., antepartum hemorrhage, preterm contractions,

insufficient placenta) would influence the fetus differently than maternally related complications (i.e., complications representing systemic diseases).

Study #2 findings: The study found that children (followed up to age 4) with uterus-related complications had a higher risk of bronchial obstruction, asthma, and allergic rhinitis compared with children without such complications. The study found that the risk of bronchial obstruction during the first two years of life and that of asthma at the age of 4 years were associated with uterus-related complication in pregnancy but not with maternally related pregnancy complications or cesarean delivery. Increasing maternal age at delivery was negatively associated with the risk of asthma and allergic rhinitis at age 4.

Study #3: Denson KWE. Passive smoking in infants, children and adolescents. The effects of diet and socioeconomic factors. International Archives of Occupational and Environmental Health 2001;74(8):525-532.

Study #3 hypothesis being tested: The diet of a mother during pregnancy or breast feeding may have greater contributory effect than ETS on the development of asthma.

Study #3 findings: Studies of ETS exposure and asthma have made little allowance for confounding by the diet of the mother and the diet of children in smoking households. Studies have linked vitamin C, vitamin E, and beta carotene deficiency to asthma. Consumption of fruit and vegetables were found to have beneficial effects on lung function. The authors suggest that smoking is often inextricably linked to other socioeconomic factors, such as diet, which may be causal factors for asthma and respiratory diseases.

Study #4: London SJ, Gauderman WJ, Avol E, Rappaport EB, Peters JM. Family history and risk of early-onset persistent, early-onset transient, and late onset asthma. Epidemiology 2001;12(5):577-83.

Study #4 hypothesis being tested: Genetic susceptibility, approximated by parental history of asthma and allergy, modulates the association between very early life exposures such as maternal smoking and the various asthma subtypes (i.e., early-onset persistent, early-onset transient, and late onset asthma).

Study #4 findings: The study found a stronger association between parental history of asthma and early-onset persistent asthma. They also found that sibling history of asthma (when in the absence of parental history) was associated with early-onset persistent asthma more than with the other subtypes. Numerous studies have shown a strong relationship between asthma risk and family history of asthma, but few have related family history to the asthma subtypes, each of which has different associations with various risk factors. The authors note that few other studies have looked at the influence of family history of asthma on the different subtypes of asthma, which differ in their associations with various risk factors.

Study #5: Peden DB. Development of atopy and asthma: candidate environmental influences and important periods of exposure. Environmental Health Perspectives 2000;108 Suppl 3:475-82.

Study #5 hypothesis being tested: Environmental agents modulate immune processes in the development of atopy and asthma.

Study #5 findings: Maternal exposure to food allergens has been linked to fetal levels of IgE and atopic development in infants. Prenatal and postnatal exposures to other allergens can affect immune processes and lead to atopic phenotype. Some studies have shown that seasonal airborne allergens prevalent in first month of life seem to predict eventual atopic disease related to that allergen later in childhood. Development of atopy is a complex immune process. In addition to any genetic predisposition that may exist, environmental agents can modulate this process and lead to expression of an atopic phenotype and development of asthma. Prenatal maternal exposures and postnatal exposures in the first year of life may have the greatest influence on the asthma development.

Study #6 Perera FP, Illman SM, Kinney PL, Whyatt RM, Kelvin EA, Shepard P, et al. The challenge of preventing environmentally related disease in young children: community-based research in New York City. Environmental Health Perspectives 2002;110(2):197-204. *(Note: This study is also cited under the research areas of childhood cancer, environmental toxicants, and neurodevelopmental disorders.)*

Study #6 hypothesis being tested: Prenatal and postnatal exposure to damage, and increased risk of cancer.

Study #6 findings: Environmental toxicants can modify the formation and maturation of the lungs. In utero sensitization to specific allergens can occur independently of maternal sensitization, putting child at higher risk for asthma. Neurochemical and behavioral effects arise from exposure to toxicants during critical windows of fetal development. Fetuses also clear toxicants less efficiently than adults and are more vulnerable to genetic damage, increasing subsequent cancer risk. Nutritional deficits in maternal diet have been linked to development of asthma in the child. Gene-environment interactions and psychosocial factors can also make a fetus or newborn more susceptible to disease. Some studies suggest that women who live in violent, crime-ridden neighborhoods experience pregnancy complications and adverse birth outcomes. Prenatal and postnatal exposure to environmental toxicants can lead to respiratory disease, impaired neurological development, genetic damage, and increased risk of cancer. Nutrition, gene-environment interaction, and psychosocial stressors are cofactors that compound the susceptibility of the fetus and newborn.

Hypothesis #4: Exposures to environmental agents found in the home, such as environmental tobacco smoke (ETS) or indoor allergens, in early childhood may lead to the development or exacerbation of asthma.

General Information Related to Hypothesis #4

- **Frequency/load of exposure to allergens:** More than 80% of asthmatic children in the U.S. are allergic, suggesting that if asthmatics are specifically sensitized to a particular allergen, exposure to high levels of that allergen may exacerbate their asthmatic symptoms.[16]
- **Frequency/load of exposure to secondhand smoke and ETS:** 29% of all homes in the U.S. permit exposure of children to secondhand smoke and 88% of all children have some level of documented exposure to ETS.[17]
- **Frequency/LoadExposure to residential risk factors:** Residential exposures (including pets, ETS, use of gas stove or oven) account for 44.4% of physician-diagnosed asthma in children 6-16 years old.[18]
- **Costs to individual/family/society/healthcare system:** There is an estimated total cost of $405 million annually (in 1997 dollars) for children and adolescents aged 6-16 who have asthma attributable to residential risk factors. Including costs for children < 6 years old, total cost increases to $807 million annually.[19]
- **Findings from recent research (targeted search):** Information reported in the following two studies contributed to the above-mentioned hypothesis.

Study #1: Lanphear BP, Kahn RS, Berger O, Auinger P, Bortnick SM, Nahhas RW. Contribution of residential exposures to asthma in U.S. children and adolescents. Pediatrics 2001;107(6):E98.

Study #1 hypothesis being tested: Residential risk factors contribute to the development of asthma.

Study #1 findings: The study found that having a pet or an allergy to a pet were the predominant risk factors for asthma. Hypersensitivity to dust mite and cockroach allergens was also a major risk factor. In addition, exposure to ETS in early childhood was found to be a risk factor for asthma. The authors found that residential risk factors accounted for 44% of physician-diagnosed asthma in children studied. An estimated 5% of children with a residential risk factor were hospitalized in the past 12 months; 40%

[16] Gold DR. Environmental tobacco smoke, indoor allergens, and childhood asthma. Environmental Health Perspectives 2000;108 Suppl 4:643-51.

[17] President's Task Force on Environmental Health Risks and Safety Risks to Children. *Asthma and the Environment: A Strategy to Protect Children*. Available at http://epa.gov/children/whatwe/fin.pdf

[18] Lanphear BP, Kahn RS, Berger O, Auinger P, Bortnick SM, Nahhas RW. Contribution of residential exposures to asthma in U.S. children and adolescents. Pediatrics 2001;107(6):E98.

[19] Ibid.

had at least one emergency department visit or clinic visit for wheezing in the past 12 months.[20]

Study #2: Gold DR. Environmental tobacco smoke, indoor allergens, and childhood asthma. Environmental Health Perspectives 2000;108(Suppl 4):643-51.

Study #2 hypothesis being tested: Environmental tobacco smoke (prenatal and postnatal exposure) and indoor allergens influence the development and exacerbation of asthma.

Study #2 findings: Prenatal (maternal smoking during pregnancy) ETS exposure can alter airway architecture and/or bronchial hyper-reactivity. Both prenatal and postnatal ETS exposure increase risk of lower respiratory illnesses and may potentiate the immune response to allergen inhalation. Studies suggest that in already allergic populations, indoor allergen exposure may increase the risk of sensitization to a specific allergen and increase risk of developing asthma. The authors suggest that ETS and indoor allergens are potential factors that influence the development of asthma through influencing the development of allergy, the expression of allergy in the lung, or the expression of bronchial reactivity. The authors note that further research is needed to evaluate the influence of the following environmental factors on development of asthma: early life infections, antibiotic use, vaccination practices, exposure to endotoxin, exposure to chronic parasitism, factors influencing gut flora, diet, obesity, a sedentary indoor lifestyle, and stress.

[20] Ibid.

Hypothesis #5: Exposure to air pollutants such as ozone and particulate matter may lead to the development or exacerbation of asthma.

General Information Related to Hypothesis #5

- **Frequency/load of exposure to ozone:** 25% of children in the U.S. live in areas in which EPA limits for ozone are regularly exceeded.[21]
- **Frequency/load of exposure to diesel exhaust particles (DEPs):** Buses, trucks, and other heavy industrial transport vehicles are major sources of ambient diesel exhaust pollution. Use of diesel fuel has increased in the U.S.: the number of miles traveled by commercial trucks has increased by 235% between 1950 and 1985. In 1996, diesel exhaust comprised a quarter of the nitric oxide (NO) smog precursors released nationally in the U.S.[22]
- **Special populations**: Children living along trucking routes or in areas of heavy trucking traffic are at a particular risk for chronic exposure to DEPs and development of asthmatic symptoms.[23]
- Exposure to ETS, NO_2, O_3, and particulate matter is higher in inner city homes. NO_2 levels are frequently in excess of U.S. EPA standards.[24]
- **Findings from recent research (targeted search):** Information reported in the following four studies contributed to the above-mentioned hypothesis.

Study #1: McConnell R, Berhane K, Gilliland F, London SJ, Islam T, Gauderman WJ, et al. Asthma in exercising children exposed to ozone: a cohort study. Lancet 2002;359(9304):386-91.

Study #1 hypothesis being tested: Children engaged in team sports in polluted communities might also be at high risk for developing asthma.

Study #1 findings: The study found that in communities with high ozone concentrations, there is an increased risk of developing asthma in children playing three or more sports compared to children playing no sports. Time spent outside was associated with a higher incidence of asthma in areas of high ozone. In areas of low ozone, sports and time spent outside had no effect. The authors suggest that exposure to ozone may modify the effects of sports on the development of asthma in some children. This exposure is dependent on air pollutant concentrations in the community and children's time spent and physical activity exerted while outside.

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21 President's Task Force on Environmental Health Risks and Safety Risks to Children. *Asthma and the Environment: A Strategy to Protect Children*. Available at http://epa.gov/children/whatwe/fin.pdf

22 Pandya R, Solomon G, Kinner A, Balmes JR. Diesel exhaust and asthma: hypotheses and molecular mechanisms of action. Environmental Health Perspectives 2002;110 Suppl 1:103-12.

23 Ibid.

24 Eggleston PA, Buckley TJ, Breysse PN, Wills-Karp M, Kleeberger SR, Jaakkola JJ. The environment and asthma in U.S. inner cities. Environmental Health Perspectives 1999107(Suppl 3):439-50.

Study #2: Pandya R, Solomon G, Kinner A, Balmes JR. Diesel exhaust and asthma: hypotheses and molecular mechanisms of action. Environmental Health Perspectives 2002;110(Suppl 1):103-12.

Study #2 hypothesis being tested: Particulate matter in diesel exhaust may play a role in causing asthma.

Study #2 findings: One study found that children living near busy diesel trucking routes have decreased lung function. A study of Italian children living on streets with heavy trucking traffic were 60-90% more likely to report asthmatic symptoms. Studies such as these indicate that exposure to DEPs are associated with inflammatory and immune responses involved in asthma, however, questions remain regarding the underlying mechanisms. The authors suggest observational studies of children be performed, including quantitative assessments of DEP exposure and airway function. They also note that research is needed to investigate the clinical relevance of the observed adjuvant effect of co-exposure to DEPs and allergens.

Study #3: Goldsmith CA, Kobzik L. Particulate air pollution and asthma: a review of epidemiological and biological studies. Reviews on Environmental Health 1999;14(3):121-34.

Study #3 hypothesis being tested: Air pollution causes exacerbation of asthma and increases asthma morbidity.

Study #3 findings: Epidemiological studies have shown a marked correlation of asthma morbidity to air pollution particle concentration. Biological studies conducted indicate that particles can increase asthmatic symptoms. Particles can affect the pulmonary environment by creating an allergic profile of cytokines and immunoglobulins, and by directly affecting lung cells. There is a substantial body of evidence indicating that air pollutants adversely affect asthmatic individuals. The authors state that more research is needed, including real-world experiments to confirm the findings of biological studies and the effects of particle exposure in conjunction with co-pollutants such as ozone.

Study #4: Eggleston PA, Buckley TJ, Breysse PN, Wills-Karp M, Kleeberger SR, Jaakkola JJ. The environment and asthma in U.S. inner cities. Environmental Health Perspectives 1999107(Suppl 3):439-50.

Study #4 hypothesis being tested: Genetic predisposition to form IgE to allergenic proteins on airborne particles is further affected by increased exposure to allergens and air pollutants and the psychosocial stresses of living in poor inner city neighborhoods.

Study #4 findings: ETS, NO_2, O_3, and particulate matter have all been shown to be in excess in inner city homes and neighborhoods and have been associated with the development and/or exacerbation of asthma. The authors suggest that genetic predisposition to allergic sensitization can lead to asthma. In addition, factors found in urban environments such as increased indoor allergens, and underlying psychosocial factors can further affect susceptibility to asthma.